REMARKS

Claims 1-20 are pending in this application. Claims 5 and 13 have been withdrawn as drawn to the non-elected invention. Claims 1-4, 6-12, and 14-20 are currently under examination in the present application. Claims 1-4, 6-12, and 14-20 have been rejected. Claims 1, 2, 6, 9, 10, 16, 19 and 20 have been amended. No new matter has been added. Applicants reserve the right to re-file this subject matter in a continuation or divisional application filed during the pendency of this application.

Rejection under 35 U.S.C. § 112(2)

Claims 16-20 stand rejected under 35 U.S.C. § 112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 stands rejected for the recitation of "defining a set of diversely modified ligands based on incremental pharmacophore changes." Specifically the examiner stated that the specification nor the claims set forth what attributes are considered "defining" and the words "diversely," "modified" and "incremental" are each relative words that the specification nor the claims provide no distinct teaching as to when the parameters of these words are exceeded, and thus the artisan could not be reasonably sure that he or she were practicing the invention.

Claim 16 has been amended to more accurately describe the method of the present invention. Specifically, claim 16(a) has been amended to describe how a set of ligands are prepared prior to screening of the ligands against a set of receptor polypeptides; hence the recitation "preparing a set of ligands, wherein each ligand is modified by step-wise pharmacophore element changes." The basis for this amendment is found on page 41 of the specification.

Claim 16 also stands rejected for the recitation of "querying the receptor polypeptides." Specifically the examiner indicated that the claims do not specify what questions or inquiries are meant to be encompassed by the query.

Claim 16(d) has been amended to more accurately define the phrase "querying the receptor polypeptides." Specifically claim 16(d) has been amended to reflect the actual method used for querying the receptor polypeptides. The basis for this amendment is found on pages 42 and 46 of the specification.

In view of the foregoing and as the "requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles" [see *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, 71 USPQ2d 1081, 1089 (Fed. Cir. 2004)], Applicants contend that claims 16-20 are definite and satisfy the requirement of 35 U.S.C. 112, second paragraph, as the components of the terms and

phrases in the claims have well recognized meanings, which allow the skilled artisan to infer the meaning of the entire phrase with reasonable confidence. Accordingly, withdrawal of the rejection is respectively requested.

Rejection under 35 U.S.C § 102(b)

Claims 1, 2, 4, 6-10, 12, and 14-20 stand rejected under 35 U.S.C. § 102(b) as anticipated by Moradpour *et al.* The examiner suggests that Moradpour *et al.* disclose a multiple inducible gene modulation system comprising a plurality of individually operable gene modulation systems wherein each individually operable gene modulation system comprises: i) one or more polynucleotides encoding a receptor complex comprising A) a DNA binding domain, B) a ligand binding domain, C) a transactivation domain; ii) a ligand and iii) a polynucleotide comprising A) an exogenous polynucleotide and B) a response element, wherein the exogenous polynucleotide is operatively linked to the response element and binding of the response element in the presence of ligand results in activation of the polynucleotide and each system is orthogonal.

The examiner suggests that the procedures disclosed by Moradpour *et al.* appear to read on the claims given their broadest possible interpretation i.e. that tet repressor is a nuclear receptor. Moradpour *et al.* describe co-expression of a tetracycline- and an ecdysone-regulated gene expression system. The claims, as amended, are directed to multiple gene regulation systems, wherein the ligand binding domains are from nuclear steroid receptors. Moradpour *et al.* describe one ligand binding domain from a nuclear steroid receptor and another ligand binding domain that is not a nuclear steroid receptor. The tet repressor is not a member of the nuclear steroid receptor family.

Moradpour *et al.* fail to teach or disclose Applicants' invention. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d, 1913, 1920 (Fed. Cir. 1989). The prior art fails to provide each and every element set forth in the present claims for the reasons set forth above.

Thus, Applicants maintain that the cited prior art fails to teach or disclose the present invention as required to set forth anticipation of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C § 103(a)

Claims 3 and 11 were rejected under 35 U.S.C. § 103(a) as unpatentable over Moradpour *et al* in view of Hofmann *et al.* The examiner suggests that Moradpour *et al.* disclose a multiple gene

modulation system of claims 1 and 9, but do not disclose a virus comprising the system and that Hofmann *et al.* teach that difficulties associated with multiple transfections of plasmids can be overcome by developing a single cassette comprising the inducible gene modulation system within a retrovirus. Therefore, one of ordinary skill in the art would be motivated to use a virus to express the gene modulation system of Moradpour *et al.*

Applicants contend that Moradpour *et al.*, for the reasons set forth above, do not teach or disclose the multiple inducible gene regulation system of claims 1 and 9 of the present invention. Hofmann *et al.* disclose a means for retroviral delivery of a single tet inducible system in one retroviral vector. Hofmann *et al.* do not teach how to construct a single retroviral vector that will contain two orthogonal gene expression cassettes for the independent expression of two genes. In fact, given the size of the 4 gene expression cassettes taught by Moradpour *et al.* two retroviral vectors would be needed (one for each system), and therefore two viral transductions would be needed in order to express the two regulation systems and the two genes in one cell. Thus, Hofmann *et al.* do not overcome the issue expressed by Moradpour *et al.* of having multiple vectors to either transfect or transduce.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). For the reasons previously presented above, Applicants contend that Moradpour *et al.* do not teach or suggest all the claim limitations of the present invention, and thus do not support a *prima facie* case of obviousness.

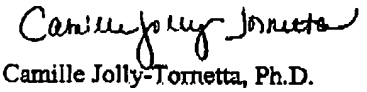
The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). In the case of Moradpour *et al.* there is no cause or suggestion to create viral vectors in order to simplify the transfection procedure. In fact, Moradpour *et al.* suggest the creation of founder cell lines already expressing the regulation systems and then introducing the genes in a single step. Therefore there is no desirability or motivation to combine those teachings with the teachings of Hofmann *et al*'s single gene viral vector system.

The above combination of prior art fails to teach Applicants' inventions and thus fails to establish a *prima facie* case of obviousness. The prior art fails to provide the required motivation. There is no suggestion or motivation in any of the cited art itself to make these combinations or to further modify these combinations.

For the reasons set forth above, Applicants maintain that the combination of the cited prior art, when the teachings are taken *as a whole*, fail to supply the motivation required to set forth obviousness of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Therefore, Applicants respectfully request reconsideration and withdrawal of all of the above rejections.

Respectfully submitted,



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